Claims

1. A method of detecting cancer-associated anti-tumour autoantibodies, which method is an immunoassay comprising contacting a sample to be tested for the presence of such autoantibodies with an immunoassay reagent and detecting the presence of complexes formed by specific binding of the immunoassay reagent to any cancer-associated anti-tumour autoantibodies present in the sample, wherein the immunoassay reagent comprises tumour marker protein prepared from bodily fluid, derived from a body cavity or space in which a tumour is or was present or with which a tumour is or was associated, of one or more cancer patients and/or tumour marker protein prepared from an excretion of one or more cancer patients wherein said tumour marker protein exhibits selective reactivity with cancer-associated anti-tumour autoantibodies.

2. A method according to claim 1 which comprises performing an immunoassay to detect and/or quantitatively measure the presence of two or more types of autoantibodies, each immunologically specific to different tumour marker proteins or to two or more epitopes of the same tumour marker protein, wherein the immunoassay is carried out using a panel of two or more immunoassay reagents, at least one of which reagents comprises tumour marker protein prepared from bodily fluid derived from a body cavity or space from one or more cancer patients and/or tumour marker protein prepared from an excretion from one or more cancer patients.

3. Use of the method of claim 1 or claim 2 for the detection or diagnosis of cancer in a patient, wherein the sample to be tested using the immunoassay is a sample of bodily fluid from taken from the patient, and wherein the presence of an elevated level of autoantibodies, as compared to normal control

individuals, is taken as an indication that the individual has or is developing cancer.

4. Use of the method of claim 1 or claim 2 in monitoring the progress of cancer or other neoplastic disease in a patient, wherein the sample to be tested using the immunoassay is a sample of bodily fluid taken from the patient, and wherein the presence of an elevated level of autoantibodies, as compared to a normal control, is taken as an indication of the presence of cancer in the patient.

5. Use of the method of claim 1 or claim 2 in detecting early neoplastic or early carcinogenic change in an asymptomatic subject, wherein the sample to be tested using the immunoassay is a sample of bodily fluid taken from the subject, and wherein the presence of an elevated level of autoantibodies, as compared to normal control individuals, is taken as an indication of early neoplastic or early carcinogenic change in the subject.

6. Use of the method of claim 1 or claim 2 in screening a population of asymptomatic human subjects to identify those subjects who are at increased risk of developing cancer, wherein the samples to be tested using the immunoassay are samples of bodily fluid taken from the subjects, and wherein subjects having an elevated level of autoantibodies, as compared to normal control individuals, are identified as being at risk of developing cancer.

7. Use of the method of claim 1 or claim 2 in monitoring the response of a cancer patient to anti-cancer treatment, wherein the sample to be tested using the immunoassay is a sample of bodily fluid taken from the patient, and wherein the presence of a decreased level of autoantibodies after treatment is taken as an indication that the patient has responded positively to the treatment.

8. Use of the method of claim 1 or claim 2 in the detection of recurrent disease in a patient previously diagnosed as having cancer, which patient has undergone anti-cancer treatment to reduce the amount of cancer present, wherein the sample to be tested using the immunoassay is a sample of bodily fluid taken from the patient, and wherein the presence of an increased level of autoantibodies in the patient, as compared to a normal control, is taken as an indication that disease has recurred.

9. Use of the method of claim 2 in the selection of an anti-cancer vaccine for use in a particular patient, wherein the immunoassay is carried out using a panel of two or more immunoassay reagents each corresponding to a different tumour marker protein in order to determine the relative strength of the patient's immune response to each of the different tumour marker proteins, wherein the tumour marker protein or proteins identified as eliciting the strongest immune response or responses in the patient is or are selected to form the basis of an anti-cancer vaccine for use in said patient.

10. A method of determining whether a vaccination procedure comprising challenging a patient with an immunogenic preparation comprising a tumour marker protein or an antigenic fragment thereof or with a nucleic acid sequence expressing said tumour marker protein, has been successful in eliciting cancer-associated antibodies to the tumour marker protein in the patient, which method is an immunoassay comprising contacting a sample of bodily fluid from the patient with an immunoassay reagent and detecting the presence of complexes formed by specific binding of the immunoassay reagent to any cancer-associated antibodies present in the sample, wherein the immunoassay reagent comprises a sample of the said tumour marker protein prepared from bodily fluid

derived from a body cavity or space in which a tumour is or was present or with which a tumour is or was associated from one or more cancer patients and/or tumour marker protein prepared from an excretion from one or more cancer patients, wherein said tumour marker protein exhibits selective reactivity with cancer-associated anti-tumour antibodies.

11. A method according to any one of claims 1, 2 or 10 wherein the bodily fluid derived from a body cavity or space is ascites fluid, pleural effusion, seroma, hydrocoele or wound drainage fluid.

12. The use according to anyone of claims 3 to 9 wherein the bodily fluid derived from a body cavity or space is ascites fluid, pleural effusion, seroma, hydrocoele or wound drainage fluid.

13. A method according to any one of claims 1, 2 or 10 wherein the excretion is urine, faeces or seminal fluid.

14. The use according to any one of claims 3 to 9 wherein the excretion is urine, faeces or seminal fluid.

15. A method according to claim 11 or 13 wherein the tumour marker protein is selected from MUC1, MUC16 or c-myc.

16. The use according to claim 12 or 14 wherein the tumour marker protein is selected from MUC1, MUC16 or c-myc.

17. A method according to any one of claims 1, 2, 10, 11 or 13 wherein the tumour marker protein is selected from c-erbB2, p53, ras, BRCA1, BRCA2, APC, PSA, CEA, and CA19.9.

18. The use according to any one of claims 3 to

9, 12 or 14, wherein the tumour marker protein is selected from c-erbB2, p53, ras, BRCA1, BRCA2, APC, PSA, CEA and CA19.9.

19. Use of tumour marker protein prepared from bodily fluid derived from a body cavity or space in which a tumour is or was present or with which a tumour is or was associated, of one or more cancer patients and/or tumour marker protein derived from an excretion of one or more cancer patients in the manufacture of an immunoassay reagent exhibiting selective reactivity with cancer-associated anti-tumour autoantibodies.

20. A method of preparing a tumour marker protein which method comprises isolating said tumour marker protein from bodily fluid wherein said fluid is:

(i) collected from a body cavity or space in which a tumour is or was present or with which a tumour is or was associated, and

(ii) said fluid represents the pooled fluid samples from two or more cancer patients.

21. A method as claimed in claim 20 wherein said fluid is acites, pleural effusion, seroma, hydrocoele or wound drainage fluid or a mixture thereof.

22. A method as claimed in claim 21 wherein said tumour marker protein is MUC1.

23. A method as claimed in claim 20 or 21 wherein said tumour marker protein is c-erbB2, p53, ras, BRCA1, BRCA2, APC, PSA, CEA, CA19.9, MUC16 or c-myc.

24. A method of preparing a tumour marker protein which method comprises isolating said tumour marker protein from a bodily fluid collected from a body cavity or space in which a tumour is or was

present or with which a tumour is or was associated wherein said bodily fluid is wound drainage fluid, seroma, hydrocoele or a mixture thereof.

25. A method of preparing a tumour marker protein which method comprises isolating said tumour marker protein from an excretion wherein:

(i) said excretion or any component thereof has been in contact with a tumour or tumour cells, and

(ii) said excretion represents pooled excretion samples from two or more cancer patients.

26. A method as claimed in claim 25 wherein said excretion is urine, faeces or seminal fluid.

27. A method as claimed in claim 25 or 26 wherein the relevant component of said excretion is bile.

28. A method as claimed in any one of claims 25 to 27 wherein the tumour marker protein is MUC 1, c-erbB2, p53, ras, BRCA1, BRCA2, APC, PSA, CEA, CA19.9, MUC16 or c-myc.

29. A method as claimed in any one of claims 20 to 28 wherein said tumour marker is purified from said fluid or excretion by affinity chromatography.

30. A method as claimed in any one of claims 20 to 29 which includes a step of removing contaminating immunoglobulin from said tumour marker protein.

31. A method as claimed in any one of claims 20 to 30 which includes a further step of immobilizing said isolated tumour marker protein to a solid support.

32. A preparation of a tumour marker protein prepared by the method of any one of claims 20 to 31

and which is substantially immunoglobulin free.

33. A kit or reagent suitable for carrying out an immunoassay which comprises a preparation of a tumour marker protein as claimed in claim 31 immobilized to a solid support.

34. A kit or reagent as claimed in claim 33 wherein said solid support is the surface of a well of a multiwell plate or is a bead.

35. A kit or reagent as claimed in claim 32 or 33 wherein said immobilized tumour marker protein is absorbed, adsorbed or covalently attached to said solid support.

36. Use of a preparation as claimed in claim 32 in the evaluation in an *in vitro* test for the therapeutic efficacy or safety of said tumour marker protein.

37. Use of a preparation as claimed in claim 32 in manufacture of a composition for the evaluation in an *in vivo* test of the therapeutic efficacy or safety of said tumour marker protein.

38. A method of calibrating an assay for measurement or detection of a given tumour marker protein in a clinical sample which method comprises the steps of:

a) preparing at least two samples of a preparation of claim 32, each of which comprises said given tumour marker protein and each of which has a different tumour marker protein concentration to each of the other said samples:

b) carrying out a quantitative measurement of the concentration of said tumour marker protein in each of said samples using

(i) a spectrophotometric method and/or,

(ii) an antibody reagent to said tumour marker protein, and

c) constructing a standard curve for a tumour marker protein concentration based on the measurements obtained in step (b).